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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,671	08/01/2001	C. Frank Bennett	RTS-0297	7102

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,671	BENNETT ET AL.	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-14* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, and 4-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Andres [PNAS Vol. 96:9873-9878, cited by applicant] and Bennett et al [US 5,988,148], Baracchini et al [US 5,801,154], Weintraub et al [Scientific American, January 1990, pages 40-46], and applicant admission on page 40.

The claimed invention is an antisense compound targeted to a nucleic acid encoding CoREST (defined by SEQ ID NO: 11). The invention also includes limitations where the compound is an antisense oligonucleotide which have various recited modifications and where the antisense compounds are included in various carriers and a method of inhibiting of CoREST in cells.

Andres et al have taught that together REST and CoREST mediate repression of the Type Ii sodium chanel promoter in neuronal cells and also that CoREST/REST complex may mediate long term repression essential to maintenance of cell identity. It is asserted at page 9877 that "[t]he details of the mechanism by which REST represses its target genes are not known.[I]t is possible that CoREST interacts and interferes with components of the basal transcriptional apparatus. [a]lternatively, CoREST could function as a repressor by recruiting, either directly or indirectly, histone deacylase activity (citations omitted). [t]he corepressors NcoR/SMRTe apparently repressthrough both mechanisms (citations omitted). [I]n this regard, it will be interesting to determine whether CoREST is independent of the NcoR/SMRTe pathway." It is clear from the

passage, for example, that the art provides a clear motivation to perform further study of the properties of CoREST. Andres et al do not teach the use of antisense oligonucleotides to inhibit CoREST.

Baracchini et al have taught, at column 6 for example, that antisense oligonucleotides can be used for research purposes and have also taught, at column 6, that antisense oligonucleotides can be modified in their sugars, backbone linkages and nucleobases and that such modifications are desirable in antisense since these modifications have desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid targets and increases stability in the presence of nucleases. Baracchini et al provide specific examples of such modifications at columns 6-8 and in Example 1, for example. These specific examples taught by Baracchini et al include phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and chimeric oligonucleotides, for example. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture, for example. Table I therefore reflects the successful practice of general antisense design taught at columns 8-10, for example. At column 4 it has been taught various carriers for antisense delivery. It has been taught at column 8 that antisense are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length, for example.

Bennett et al have taught general targeting guidelines at columns 3-4, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example. It has been taught in column 5, for example, that antisense compounds are commonly used as research

reagents and diagnostics, for example. At column 5 it has been taught that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. At columns 6-7 it has been taught preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, for example. At columns 7-8 it has been taught that preferred antisense oligonucleotides comprise modified sugar moieties including2'-O-methoxyethyl. It has also been taught to modify nucleobases in antisense oligonucleotides at column 8-9 which includes the teaching of 5-methyl cytosine and at column 10 it has been taught chimeric antisense oligonucleotides. All of the above referred to modification are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. At columns 10-24, for example it has been taught numerous "carriers" for antisense oligonucleotides. In table I it has been taught the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification).

Weintraub has taught that one in the art can use antisense oligonucleotides to elicit information about a given genes function.

At page 40 of the instant specification it is admitted that the antisense of the invention were designed based on the published sequence of CoREST referenced as (SEQ ID NO:11).

It would have been obvious to make antisense oligonucleotides as claimed since the prior art has asserted that there is more information that needs to be learned about CoREST function. The prior art has also taught that antisense oligonucleotide are

versatile tools for the elucidation of gene function and that antisense can be designed based on a known sequence with a reasonable expectation of success. Furthermore the art has taught various modification and carriers for antisense oligonucleotides that all provide advantages for their use in cell, for example. The art has therefore provided a clear motivation to make the invention as claimed.

The invention as a whole would therefore *prima facie* obvious to one in the art at the time the invention was made.

Applicant's arguments filed 3/23/04 have been fully considered but they are not persuasive.

It is noted that applicant has pointed out that the examiner misidentified SEQ ID NO: 11 as GenBank AI922671 which is SEQ ID NO: 12. However the fact remains that applicant admits the sequences were published, see line 22. Furthermore it is clear that the sequences are all directed to a nucleic acid encoding CoRest. It is clearly a reasonable interpretation to read the claim to read on a nucleic acid that encodes the CoRest encoded by SEQ ID NO: 11, since, for example, the antisense oligonucleotides of claim 3, which clearly must be embraced by the scope of claim 1, are targeted to several different SEQ ID NOS: that encode the human CoRest, for example.

Applicant argues improper hindsight and asserts that no teaching or suggestion to combine has been provided. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction

based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Applicant argues that the Bennett and Baracchini references are specific to only those specific targets in the Patent references. However it is noted that both Patent teach the same methods for antisense design in both patents, which clearly demonstrates the general nature of those teachings. The rejection provides a reference that asserts that the target gene of the instant invention is in need of more study to determine biological properties of the target. A general reference is provided that indicates that the function of any gene can be studied via the use of antisense. Two other references are provided that teach specifically how to make and use antisense with a clear expectation of success where the references also teach that antisense is a nice tool for studying gene function, for example.

Applicant argues that the references provide at best a generalized incentive insufficient to render obvious the claimed species. Applicant asserts that the art would not teach those that specifically bind and inhibit. It is maintained that the references supplied, when combined as in the rejection would clearly make the claimed invention where the antisense bind and inhibit. It is noted that the specification is quite loose in its definition of what is specific, for example. Applicant argues that the species included in the invention includes a vast number of possibilities. It is noted that one in

the art is quite reasonably assured by the prior art to find at least one of those vast possibilities based on the teachings in the cited prior art.

Applicant also argues that the expectation of success has not been established, however the prior art references of Bennett and Baracchini and Weintraub would indicate otherwise.

Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and eliminating reference to non-elected subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SRM

SEAN McGARRY
PRIMARY EXAMINER
1635